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The role of serum 25 hydroxy Vitamin D level in asthmatic children in Al Diwaniyah maternity and children teaching Hospital .

A clinical study in Al Diwaniyah maternity and children teaching Hospital.

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الخلاصة

خلفية الدراسة: أظهرت الدراسات الحديثة أن نقص فيتامين D وقصوره شائعاً في جميع أنحاء العالم، ويرتبط مع العديد من الأمراض بما في ذلك الربو.

هدف الدراسة: لتقييم قصور فيتامين D والعواقب السريرية في الأطفال الذين يعانون من الربو.

طريقة العمل: أجريت هذه الدراسة على 173 أطفال، كان 87 طفلاً يعانون من الربو و86 طفلاً كالمعتاد المجموعة الضابطة، الذين تتراوح أعمارهم بين 2 إلى 5 سنوات في الديوانية، العراق، خلال الفترة من 17-9 سبتمبر إلى 3-11 نوفمبر عام 2014. تم قياس مستويات 25 - هيدروكسي فيتامين دي ومقارنته بين المجموعتين. تم تقييم شدة الربو ومستويات السيطرة على الربو وفقاً للمبادرة العالمية لبرنامج العلاج والوقاية من الربو (GINA).

النتائج: كان فيتامين D أقل بكثير في مرضى الربو من في المجموعة الضابطة ($P < 0.001$). يعني فيتامين D في مرضى الربو كان (37.5 ± 7.43) ، بمتوسط (5.5) ومعدل (2-392). يعني فيتامين D في الضابطة كان (173.88 ± 17.79) ، بمتوسط (109.15) ومعدل (590 - 2.4).

النتائج: الفرق بين متوسط مستويات فيتامين D في مجموعة الربو (يعني ± 37.5 SD) + 7.43 نانوغرام / مل والمجموعة الضابطة الصحية (يعني $\pm 173.88 \pm 17.79$ SD) نانوغرام / مل وجد أن تكون ذات دلالة إحصائية ($P = 0.003$). ولوحظ وجود اختلاف كبير بين المجموعتين فيما يتعلق تردد من التهابات الجهاز التنفسي مما يؤدي إلى مراجعة وحدة الطوارئ وعدد من المستشفيات ($P < 0.001$).

الاستنتاجات: أظهرت هذه النتائج أن مستويات المصل 25-هيدروكسي فيتامين D ارتبطت عكسياً مع شدة الربو أي علاقة مباشرة وهامة بين مستويات فيتامين D وشدة الربو.

Abstract

Background: recent studies showed that vitamin D deficiency and insufficiency are common worldwide and associated with many diseases including asthma.

Aim of study: to evaluate vitamin D insufficiency and deficiency and its clinical consequences in children with asthma in Al Diwaniyah maternity and children teaching Hospital .

Methods: This a case-control study was carried out on 173 child, 87 had asthma and 86 normal children as control group, aged 2 to 5 years in Al Diwaniyah maternity and children teaching Hospital, Iraq, during the period from the 17th of September to 3rd of November 2014. Serum 25-hydroxy vitamin levels were determined and compared between the two groups.

Results: The difference between mean vitamin D levels in the asthmatic group (mean \pm SD) 37.5 ± 7.43 ng/mL and the healthy control group (mean \pm SD) 173.88 ± 17.79 ng/mL was found to be statistically significant ($P=0.003$). Mean vitamin D was significantly lower in asthmatic patients than in control subjects ($P<0.001$).

Mean vitamin D in asthmatic patients was (37.5 ± 7.43), with a median of (5.5) and a range of (2-239). Mean vitamin D in control subjects was (173.88 ± 17.79), with a median of (109.15) and a range of (4.2-590).

A significant difference was observed between the groups regarding the frequency of respiratory tract infections leading to emergency unit admissions and number of hospitalizations ($p < 0.001$).

Conclusion: these results showed that serum 25-hydroxy vitamin D levels were inversely associated with asthma severity i.e direct and significant relationship between vitamin D levels and severity of asthma.

Introduction

Vitamin D Physiology :

Vitamin D is a fat soluble vitamin. recently, research has found that vitamin D may play a role in multiple chronic diseases such as cancer, autoimmune diseases, infections, and cardiovascular disorders. Vitamin D may also have a role in several diseases involving the respiratory system. (1). Vitamin D Physiology is shown in figure 1.

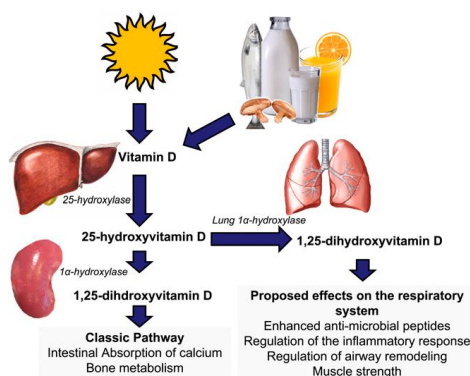


Figure1:-Vitamin D Physiology(2)

Food Sources of Vitamin D

There are few natural dietary sources of vitamin D. Fish liver oils have a high vitamin D content. Other good dietary sources include fatty fish and egg yolks. Most children in industrialized countries receive vitamin D via fortified foods, especially formula and milk (both of which contain 400 IU/L) and some breakfast cereals and breads). Breast milk has a low vitamin D content, approximately 12-60 IU/L . The child daily mean period of exposure to sunlight was determined. Exposure of 10 minutes between the hours of 10:00Am and 15:00Pm was thought to provide approximately 2000-3000 IU of Vitamin D (3) .

Asthma

Asthma is a chronic inflammatory condition of the lung airways resulting in episodic airflow obstruction. Asthma severity is the intrinsic intensity of disease, and assessment is generally most accurate in patients not receiving controller therapy. Hence, assessing asthma severity directs the initial level of therapy. The 2 general categories are intermittent asthma and persistent asthma, the latter further subdivided into mild, moderate, and severe. (4)

Role of vitamin D in asthma:-

vitamin D helps in lung maturation and airway inflammation in early transient wheezier ,where as in episodic wheezier it provides anti-viral immunity and reduces the attack of wheeze. Lower level are associated with increase markers of allergy and asthma severity. Insufficient level are associated with risk of sever exacerbation particularly when not on inhaled corticosteroid. Deficiency level of vitamin D is associated with increased airway hyper responsiveness, lower pulmonary functions and worse asthma control. (5)

1.2 Aim of the study:-

To evaluate vitamin D insufficiency and deficiency and its clinical consequences in children with asthma in Al Diwaniyah maternity and children teaching Hospital .

2-Patients And Methods

To achieve the aim of the present study , a case-control study design was adopted. All the patients should fulfill the inclusion criteria were included in the study .The study was conducted in Maternity and children teaching hospital in Al-Diwaniyah Governorate, Republic of Iraq. The Data collection was carried out during the period from the 17th of September to 3rd of November 2014. Study participants were carried out on 173 children aged (2-5) years(87 asthmatic patients and 86 control).

Inclusion criteria:

The subjects included 87 asthmatic patients, diagnosed according to the Global Initiative for Asthma management and prevention(GINA) criteria (6):-

- a physician's diagnosis of asthma as :-

- 1- symptoms of recurrent (i.e. more than two in previous six months) episodes of wheezing, cough, shortness of breath, or a combination of these.
- 2- documented reversibility with bronchodilators.
- 3- symptoms of and/or use of medication for asthma in the previous six months. The control group included 86 children aged (2-5) years who came to the Pediatric Outpatient Clinic at the same hospital and who were previously healthy and did not suffer from any acute or chronic illnesses such as allergy, asthma or other respiratory tract infections.

Exclusion criteria

- Those receiving vitamin D therapy subsequent to any disease.
- Those receiving anti-epileptic therapy.
- Those receiving long-term steroid treatment besides asthma treatment were excluded from the study, as were those with chronic diseases other than asthma, such as lung disease, renal diseases, liver diseases and endocrine disease.

The questionnaire and data collection:

The questionnaire which had been used consisting of 2 parts:

- A-** First part was socio -demographic characteristics which included (name, age, sex, residence, economic status) .
- B-** Second part was measurements such as height and weight were recorded during meetings with the children's family.
- C.** The child's daily mean period of exposure to sunlight was roughly assessed.

D. Vitamin D intake was estimated using a food frequency questionnaire, and questions were asked about children's eating habits of vitamin D-rich and vitamin D enriched foods.

E. Questions were asked about the number of respiratory tract diseases had experienced in the previous 6 months, the number of emergency admissions and hospitalizations and the number of asthma attacks.

2 .Laboratory Investigation: The plasma concentration of vitamin D was assayed using an electrochemiluminescence immunoassay on the Biotek ELx50auto analyser (Americans). When vitamin D serum level was less than (3.75 ng/ml), subjects and patients were labeled as deficient. When vitamin D serum level was more than (6.25 ng/ml), subjects and patients were considered normal. Any level between the above mentioned figures was considered vitamin D insufficiency (7).

Statistical analyses -

Statistical analysis was done by using SPSS (statistical package for social sciences) version (16) computer soft ware of Excel2007 . A level of significance of less than 0.05 was considered as statistically significant.

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General 3-Results**characteristics of the study sample**

Mean age of control group was (**3.49+0.13 year**), while mean age of asthmatic group was (**3.83+0.12year**). There was no statistical difference in mean age between asthmatic patients and control group, ensuring a statistical match between study groups.

Asthmatic patients were heavier and had a significantly higher BMI mean compared to control group, (**15.82+0.23**) versus (**15.14+0.19**), respectively; P-value was (**0.016**). These results are outlined in table (1).

Table 1: General Characteristics of asthmatic group and control group

Characteristic	Control (n = 86)		Asthma (n = 87)		P
	Mean	SE	Mean	SE	
Age	3.49	0.13	3.83	0.12	0.051
Height	101.92	1.30	103.91	1.50	0.320
Weight	15.81	0.38	17.22	0.48	0.022
BMI	15.14	0.19	15.82	0.23	0.016

There was no significant difference in sex ratio between asthmatic patients and control subjects, (**1:1.29** versus **1.21:1**); P-value was **0.149**.

Table 2: Gender distribution of asthmatic patients and control subjects

Gender	Control		Asthma	
	No.	%	No.	%
Male	47	54.65	38	43.68
Female	39	45.35	49	56.32
Total	86	100.00	87	100.00

P=0.149

Classification of patients and control subjects according to economic status

The percentage of patients with poor economic status was (**33.33 %**), while percentage of control subjects with poor economic status was (**13.95%**). Poor economic status was significantly more frequent in asthmatic patients (**P=0.003**). Table (**3**) shows these results.

Table 3: Classification of patients and control subjects according to economic status

Economic status	Control		Asthma	
	No.	%	No.	%
Average	74	86.05	58	66.67
Poor	12	13.95	29	33.33
Total	86	100.00	87	100.00

X²=8.983; Df=1

P=0.003

Comparison of mean Vitamin D between asthmatic patients and control group

Mean vitamin D was significantly lower in asthmatic patients than in control subjects (**P<0.001**). Mean vitamin D in asthmatic patients was (**37.5+7.43**), with a median of (**5.5**) and a range of (**2-239**). Mean vitamin D in control subjects was (**173.88+17.79**), with a median of (**109.15**) and a range of (**4.2-590**).

Table (**4**) and figure (**2**) shows a comparison of mean serum vitamin D between both groups.

Table 4: Mean Vitamin D between Asthmatic patients and Control group

Control (n = 86)				Asthma (n = 87)				P
Median	Mean	SE	range	Median	Mean	SE	range	
109.15	173.88	17.79	4.2-590	5.50	37.50	7.43	2-391	<0.001

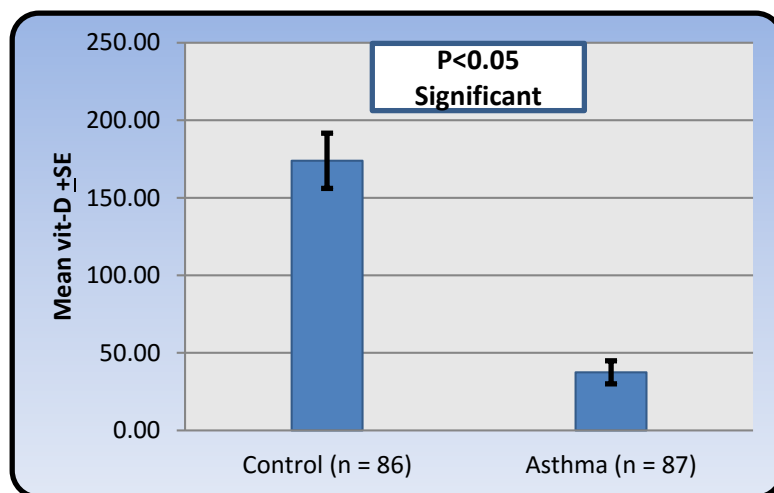


Figure 2: Mean Vitamin D between Asthmatic patients and Control group

Patients with vitamin Deficiency were limited to asthmatic group, while vitamin D insufficiency was more frequent among patients than control subjects. This difference was statistically significant ($P<0.001$).

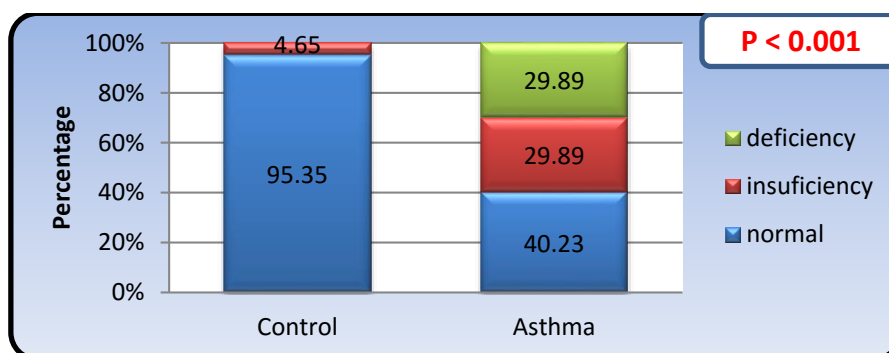


Figure 3: Number and percentage of patients and control with vitamin D deficiency and insufficiency.

Table 5: Number and percentage of patients and control with vitamin D deficiency and insufficiency.

Vitamin D	Control		Asthma	
	No.	%	No.	%
Deficiency	0	0.00	26	29.89
Insufficiency	4	4.65	26	29.89
Normal	82	95.35	35	40.23
Total	86	100.00	87	100.00

$\chi^2=61/01$; Df =2

$P<0.001$

Correlation between frequency of symptoms and Vitamin D

There was a significant negative correlation between serum vitamin D and number of recurrent wheezing, cough and shortness of breath, whether in terms of day/week (WCSDW) or in terms of night /month (WCSNM).

Also there was a significant negative correlation between number of hospital admission /in previous 6 month and serum vitamin D in asthmatic patients. These findings are shown in figures (4, 5 and 6).

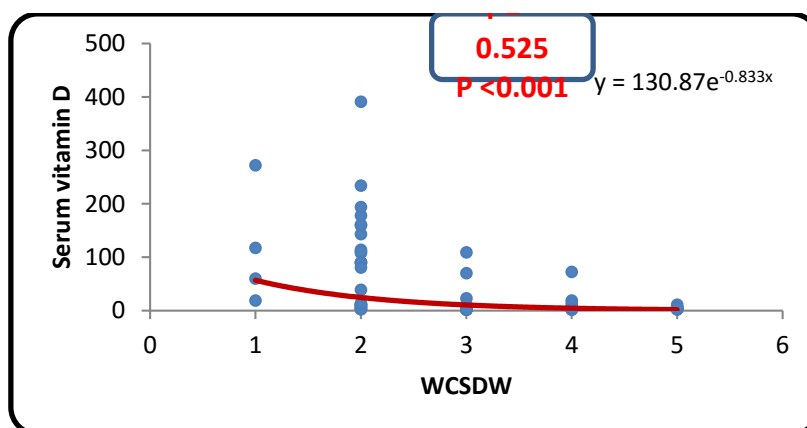


Figure 4: Correlation between frequency of symptoms (day/week) and serum vitamin D in asthmatic patients

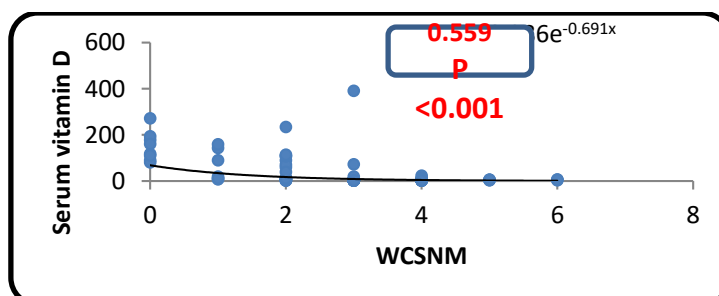


Figure 5: Correlation between frequency of symptoms (night/month) and serum vitamin D in asthmatic patients

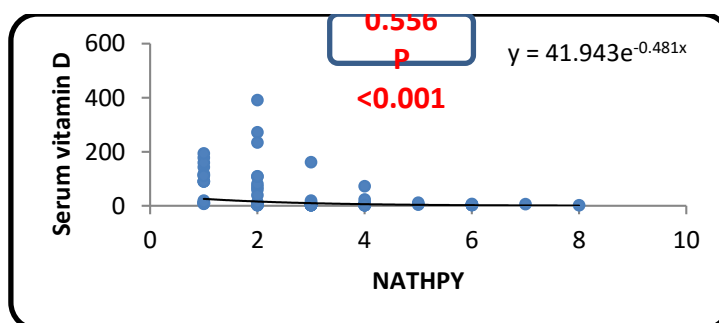


Figure 6: Correlation between number of hospital admission / previous 6 month and serum vitamin D in asthmatic patients.

Correlation between vitamin D and severity of attack

Mean serum vitamin D showed significant decrease with more severe attack of asthma. Mean serum vitamin D was (114.29+20.8) in patients with intermittent attacks. Mean serum vitamin D was (30.92+11.19) in patients with persistent mild attacks. Mean serum vitamin D continued to decrease in patients with intermediate persistent attack to be (7.26+2.43). It reached its lowest level in patients with severe persistent attack to be (5.83+0.52). These findings are outlined in table (6) and figure (7).

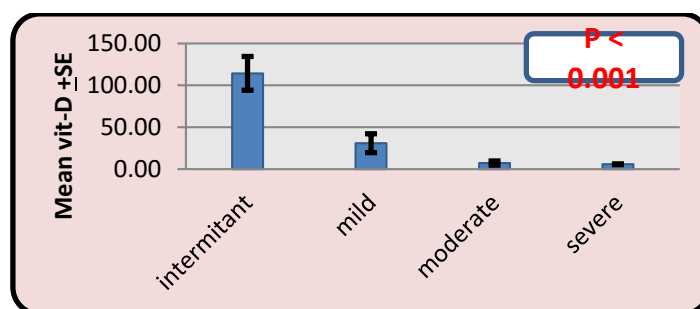


Figure 7: Correlation between vitamin D and severity of attack.

Table 6: Correlation between vitamin D and severity of attack.

	Severity of attack									
	Intermittent		mild		moderate		severe		Total	
Vitamin D	No.	%	No.	%	No.	%	No.	%	No.	%
Normal	16	100.00	14	35.90	4	13.79	0	0.00	35	40.23
Insufficiency	0	0.00	12	30.77	12	41.38	0	0.00	26	29.89
Deficiency	0	0.00	13	33.33	13	44.83	3	100.00	26	29.89
Total	16	100.00	39	100.00	29	100.00	3	100.00	87	100.00

Discussion

The present study investigated the level of vitamin D in asthmatic patients and assess the correlation of vitamin D with different variable. In our study, asthmatic patients were heavier and had a significantly higher BMI mean compared to control group P-value was (0.016). These results are outlined in table (1).

Our study showed There is no significant difference in sex ratio between asthmatic patients and control subjects, P-value was 0.149. These results are outlined in table (2). In table (3) we noticed Poor economic status was significantly more frequent in asthmatic patients (P=0.003). In our study, vitamin D insufficiency and deficiency were found to be significantly higher in asthmatic children than in the control group Table (4) and figure (2) shows these results., and these values were lower than values reported in other studies.

In our study sufficient, insufficient and deficient accounted as 40.23%, 29.89%, and 29.89% of the subjects respectively. Studies conducted in the Middle East, in Italy (8), and in the Costa Rica (9) showed similar results, whereas the percentages found in a study in Iran were respectively higher (84%, 12% and 4%) (10).

In our study Patients with vitamin Deficiency were limited to asthmatic group, while vitamin D insufficiency was more frequent among patients than control subjects (P<0.001), table (3) and figure (2) shows these results. Vitamin D is involved in the

maintenance of immune homeostasis. It has an important role in innate immunity; particularly through the direct induction of antimicrobial peptide (cathelicidin) gene expression. Vitamin D promotes the induction of T regulatory cells, including the expression of inhibitory cytokines (IL-10 and TGF β) and control of CD4-positive T lymphocytes (Th1 and Th2). (11)

In figures (4 and 5) shows there is a significant negative correlation between serum vitamin D and number of recurrent wheezing, cough and shortness of breath, whether in terms of day/week (WCSDW) or in terms of night /month (WCSNM). These results are consistent with studies in children (13) and adults (14) with asthma.

When analysing the number of hospital admission of the previous 6 month, we observed that was a significant negative correlation between number of hospital admission / previous 6 month and serum vitamin D in asthmatic patients, showed in figure (6). Alyasin et al. found no relationship between vitamin D levels and hospitalizations (15). In fact, vitamin D deficiency has been shown to predispose children to respiratory infections and vitamin D supplements have been shown to decrease the incidence of respiratory infections . That's explain vitamin D exerts many of its effects through contact with vitamin D receptors which have been found in a variety of cells, including lung cells and many cells of the immune system (16).

The finding that most tissues and cells in the body have vitamin receptors and that several possess the enzymatic apparatus to synthesise the active form 1,25-dihydroxyvitamin D from the primary vitamin D, 25-hydroxyvitamin D, has provided new insight into the role of this vitamin deficiency in several diseases including Asthma, led us to think that there were other factors and mechanisms determining serum vitamin D levels in asthmatic patients (17).

Conclusions

In summary, in our study we tried to clarify the role of vitamin D in asthma we found lower serum 25(OH) D levels in asthmatic children compared with controls, and we also found a direct relationship between serum 25(OH) D levels and severity of asthma. Exposure to sunlight and a diet rich in vitamin D increased the vitamin D levels in both asthmatic and healthy children.

Recommendation

- An interventional study in asthmatic patients with low serum vitamin D - concentration may establish a causal relationship between asthma and vitamin D
- Improvement of nutritional status of asthmatic patients.

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